Comments on the general and specific aspects on the Review relative to OPUL-1001US:

1. OPUL-1001US patent based on a system of components & units, which comply with regulatory requirements of the US FDA requirements, including 21 CFR Part 11. These requirements have underlined the specification, design, and implementation of the system. The Reference could not have anticipated these requirements during the time of their development & submission, as some of the key rules, such as 21 CFR Part 11 did not exist. Furthermore, there are significant semantic differences in the Reference patent used for rejection and ours; - specific to these in OPUL-1001US patent:

   1.1. page 1/20-25: see, qualification controls..... , this is a requirement of the US FDA, which is not described or claimed in the Reference

   1.2. The OPUL-1001US patent utilizes multiplexing for both the control unit and the oscillator, whereas the Reference includes multiplexing only for the control unit. The 96-well microplate array measurement cannot be solved by the Reference multiplex technology, whereas the OPUL-1001US patent with the dual multiplexing can.

   1.3. page 1/25-35...validation & qualification controls.." NOTE: It is universally accepted, that instrument validation and integrated software validation

cannot be derived from general solutions as described in the Reference to comply with US FDA requirements, in particular with 21 CFR Part 11, and it is not self evident from the Reference, as how to "build" one. Furthermore, calibration described in the reference is for a particular analytical methodology and not necessarily suitable for the system (i.e., instrumentation & software), as required to comply with US FDA requirements, in particular with 21 CFR Part 11, or can be derived from the Reference without the utilization of specific technology needed to be invented.

1.4. page2/1-5: "....robustness..." is another US FDA criteria in the validation of a particular system, which is not described or claimed in the Reference or can be derived from the Reference without the utilization of specific technology needed to be invented.

1.5. page3/Fig 2 & Fig 6 relative to temperature control: Reference describes temperature regulation only for the sample holder and not above the sample, which together create a closed sample space with differential temperature regulation for the benefit of eliminating evaporation and/or condensation of the sample solution, and to ensure that quantitative measurements are reliable. Furthermore, additional benefit is the appropriate coating of the temperature controlled cover with various materials to block selectively the light penetration, which could affect the integrity of the sample. The Reference makes no such statement or claim. Furthermore, the closed system allows gas purging or the injection of gases to activate a particular reaction or to induce mixing for homogeneity. None of the above can be derived from

the Reference by a knowledgeable person, it must be invented and the Reference modified accordingly.

1.6. page3/Fig 2 & Fig 6 relative to temperature measurements: the OPUL-1001US patent utilizes directly mounted Pt micro-sensor on the resonating crystal, whereas the Reference utilizes indirect measurement as far as the reaction temperature. The methodology used by the Reference is unable provide reliable temperature measurements, as the quartz crystal is a very poor heat conductor.

1.7. Page4/Fig. 17: describes automatic sample loading, which cannot be found in the Reference or derived from the Reference.

1.8. Page5/20-35 – we state: "…. Quality control..." application for the regulated industries, such pharmaceutical, clinical, biotechnology, which require US FDA regulatory compliance. The compliance requirements are not stated in the Reference, and based on the description and claims in the Reference they cannot be derived without the invention of the necessary & sufficient arts & science.

1.9. Page 6/1-5: "….pollutants…." the determination of which requires the compliance of another federal regulatory agency, the EPA, which requires the specification, design, and implementation of compliant system.

1.10. page 7/2-12: temperature profile can be mapped for both the sample chambers & the sample covers. The Reference does not describe and/or states such

claims, and they cannot be derived without the need of additional invention to meet regulatory compliance.

1.11. Page 7/30-35: the cover in addition to the temperature regulation, protective effect from light radiation, prevention of evaporation and/or condensation, creation of closed environment with variable capability, it also protects the samples from contamination. The Reference does not describe and/or states such claims, and they cannot be derived without the need of additional invention to meet regulatory compliance.

1.12. page 8/5-15: multi-dimensional thermal fluctuation can be used for various sample kinetics and reaction studies. The Reference does not describe and/or states such claims, and they cannot be derived without the need of additional invention to meet regulatory compliance.

1.13. page 9/1-6: the above technology thermal regulation and contamination control supports suitable environment for aerobic and aenorobic testing, including bioburden and endotoxin. The Reference does not describe and/or states such claims, and they cannot be derived without the need of additional invention to meet regulatory compliance.

1.14. page 9/28-33: describes the utilization of Fourier Transform Frequency generator for "sample fingerprint." The Reference does nor describe Fourier Transform Frequency generator and/or states such claims, and they cannot be derived without the need of additional invention to meet regulatory compliance.

1.15. page 10/25-28: describes the utilization of the unique combination of upper cover and sample block temperature, which supports the determination of dew point by crystal embedding in the upper cover, which through correlation improves the accuracy, precision and reproducibility of the measurements. The Reference does not describe and/or states such claims, and they cannot be derived without the need of additional invention to meet regulatory compliance. Furthermore, this dual measurement technology is suitable for biofilm measurement, whereas no such capability exists in the Reference.

1.16. page14/20-34 & page 15/10-12: describes 3-dimensional detector architecture, whereby a single detector is fabricated to hold several sub-detectors for a multi-fold & multi-dimensional detector assembly. The Reference does nor describe and/or states such claims, and they cannot be derived without the need of additional invention to meet regulatory compliance

1.17. page 15/16-33, page 16/1-17 & Fig. 17: describes the application of continuous flow system for even higher throughput measurements. The Reference does not describe and/or states such claims, and they cannot be derived without the need of additional invention to meet regulatory compliance.

1.18. page 17/7-14: describes a NIST & FDA compliant calibration for the system. The Reference does not describe and/or states such claims, and they cannot be derived without the need of additional invention to meet regulatory compliance.

1.19. page 17/15-20: describes crystal suitability methodology. The Reference does not describe and/or states such claims, and they cannot be derived without the need of additional invention to meet regulatory compliance.

1.20. page 17/21-32: describes maintenance of the detector and verification. The Reference does not describe and/or states such claims, and they cannot be derived without the need of additional invention to meet regulatory compliance.